AMENDMENTS TO THE CLAIMS

Docket No.: 05432/1200028-US1

The following listing of claims replaces all prior listings of claims presented in the application:

1 (Currently amended). A method of preparing THIP 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol comprising the steps:

a) reacting a compound of formula (2)

with an alkylating agent of formula (3)

$$R^2$$
 C
 H
 (3)

wherein R^2 and R^3 are independently selected from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, aryl, or heteroaryl, optionally substituted with a C_{1-12} alkyl, C_{1-12} alkoxy, or aryl, and

L is a leaving group,

to obtain a quarternary salt of formula (4)

 $\mathbb{R}^2 \stackrel{\mathsf{CH}}{\underset{\mathsf{R}^3}{\mid}}$

wherein L, R² and R³ are as defined above,

b) reacting the quarternary salt of formula (4) with a mild reducing agent to obtain a compound of formula (5)

wherein R² and R³ are as defined above,

c) reacting a compound of formula (5) with a reagent of formula (6a)

 $\label{eq:continuous} wherein \ R' \ is \ C_{1\text{--}12} \ alkyl, \ C_{2\text{--}12} \ alkenyl, \ C_{3\text{--}8} \ cycloalkyl, \ C_{3\text{--}8} \ cycloalkenyl, \ acyl, \ or \ aryl$ optionally substituted with one or more $C_{1\text{--}12} \ alkyl, \ C_{1\text{--}12} \ alkoxy, \ or \ aryl,$

X is a leaving group,

Y is O or S,

Z is O, S or C_{1-6} alkyl,

optionally followed by reaction with a nucleophile,

to obtain a mixture of a compound of formula (7a) and a compound of formula (7b)

$$R'Z$$
 Y
 ZR'
 $R'Z$
 $(7a)$
 $R'Z$
 $(7b)$

wherein Y, Z, and R' are as defined above,

d) reacting the mixture of (7a) and (7b) with a nucleophile, followed by acidification, to obtain a compound of formula (8a)

wherein Y, Z, and R' are as defined above, and

- e) reacting a compound of formula (8a) with an acid to obtain THIP 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol as an acid addition salt.
- 2 (Previously presented). The method of claim 1 wherein step a) is carried out in a polar solvent.
- 3 (Previously presented). The method of claim 1, wherein in the alkylating agent of formula (3), R^2 and R^3 are independently selected from H, methyl, ethyl, allyl, phenacyl, phenyl, or methoxyphenyl and

L is selected from Br, Cl, I, OMs, or OTs.

- 4 (Original). The method of claim 3, wherein the alkylating agent of formula (3) is selected from MeI, EtI, BzBr, p-CH₃OC₆H₄CH₂Br, allylBr, and the corresponding mesylates (OMs) and tosylates (OTs).
- 5 (Previously presented). The method of claim 1 wherein the reduction in step b) is carried out in alcohol and water.
- 6 (Previously presented). The method of claim 1 wherein the mild reducing agent in step b) is LiBH₄ or NaBH₄.

7 (Previously presented). The method of claim 1, wherein in the reagent of formula (6a), R' is C_{1-12} alkyl, C_{2-12} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, or aryl optionally substituted with a C_{1-12} alkyl, C_{1-12} alkoxy, or aryl,

X is selected from Cl, Br, I,

Y is O or S,

Z is O or S.

8 (Previously presented). The method of claim 7, wherein the reagent of formula (6a) is selected from C_{1-12} alkyl chloroformate.

9 (Previously presented). The method of claim 1, wherein a compound of formula (5) is first protected as a carbonate or carbamate and then reacted with the reagent of formula (6a) in step c).

10 (Previously presented). The method of claim 1, wherein the nucleophile in step d) is a soft nucleophile in an aqueous or organic solution.

- 11 (Currently amended). The method of claim 1, wherein the reaction with a nucleophile in step d) is followed by acidification by adjusting pH to $[[\le 5]] \le 5$.
- 12 (Previously presented). The method of claim 1, wherein in step d), reaction with the nucleophile in an aqueous solution is followed by separating the aqueous phase, followed by acidification with an aqueous acid, and extraction into an organic phase.
- 13 (Previously presented). The method of claim 1, wherein, prior to step e), a compound of formula (8a) or a salt thereof is purified by a process of extraction from one phase to another.
- 14 (Currently amended). The method of claim 1, wherein in step d) a compound of formula (8a) is obtained in high at a purity of more than 98% according to HPLC.

15 (Previously presented). The method of claim 1, wherein step e) is carried out using a mineral acid.

16 (Previously presented). A method of preparing a compound of formula (2)

comprising reacting the compound of formula (10)

with a dehydrating agent, to obtain the compound of formula (2).

17 (Original). A compound of formula (2)

or a salt thereof.

18 (Currently amended). A method of preparing THIP 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol comprising reacting a compound of formula (8a) or a salt thereof

wherein R' is C_{1-12} -alkyl, C_{2-12} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, or aryl optionally substituted with one or more C_{1-12} alkyl, C_{1-12} alkoxy, or aryl,

Y is O or S, and

Z is O, S or C₁₋₆ alkylene,

with an acid to obtain THIP 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol as an acid addition salt.

19 (Currently amended). A compound of formula (8a)

wherein R' is C_{1-12} -alkyl, C_{2-12} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, or aryl optionally substituted with one or more C_{1-12} alkyl, C_{1-12} alkoxy, or aryl,

Y is O or S,

Z is O, S or C₁₋₆ alkyl, or

a salt thereof.

20 (Currently amended). A method of preparing THIP 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol comprising the steps:

a) reacting a compound of formula (2)

with an alkylating agent of formula (3)

$$R^2$$
 C
 H
 (3)

wherein R^2 and R^3 are independently selected from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, aryl, or heteroaryl, optionally substituted with a C_{1-12} alkyl, C_{1-12} alkoxy, or aryl, and

L is a leaving group,

to obtain a quarternary salt of formula (4)

wherein L, R² and R³ are as defined above,

b) reacting the quarternary salt of formula (4) with a mild reducing agent to obtain a compound of formula (5)

wherein R² and R³ are as defined above,

c2) reacting [[a]] the compound of formula (5) with a reagent of formula (6b)

wherein R is C_{1-12} alkyl, C_{2-12} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, or aryl optionally substituted with one or more C_{1-12} alkyl, C_{1-12} alkoxy, or aryl,

U is N or CR¹, wherein R¹ is H or R,

W is O, S or NR⁴, wherein R⁴ is H or R,

optionally followed by reaction with a nucleophile,

to obtain a mixture of a compound of formula (7c) and a compound of formula (7d)

wherein R is C_{1-12} alkyl, C_{2-12} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, or aryl optionally substituted with one or more C_{1-12} alkyl, C_{1-12} alkoxy, or aryl,

U' is N or CR¹, wherein R¹ is H or R,

W is O, S or NR⁴, wherein R⁴ is H or R,

d2) reacting the mixture of (7c) and (7d) with a nucleophile, followed by acidification, to obtain a compound of formula (8b)

wherein W, U', and R are as defined above,

- e2) reacting a compound of formula (8b) with an acid to obtain THIP 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol as an acid addition salt.
- 21 (Previously presented). The method of claim 20 wherein step a) is carried out in a polar solvent.
- 22 (Previously presented). The method of claim 20, wherein in the alkylating agent of formula (3), R² and R³ are independently selected from H, methyl, ethyl, allyl, phenacyl, phenyl, or methoxyphenyl and

L is selected from Br, Cl, I, OMs, or OTs.

- 23 (Original). The method of claim 22, wherein the alkylating agent of formula (3) is selected from MeI, EtI, BzBr, *p*-CH₃OC₆H₄CH₂Br, allylBr, and the corresponding mesylates (OMs) and tosylates (OTs).
- 24 (Previously presented). The method of claim 20 wherein the reduction in step b) is carried out in alcohol and water.
- 25 (Previously presented). The method of claim 20 wherein the mild reducing agent in step b) is LiBH₄ or NaBH₄.

26 (Previously presented). The method of claim 20, wherein in the reagent of formula (6b), R is C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkenyl, acyl, or phenyl optionally substituted with a C₁₋₆ alkyl, C₁₋₆ alkoxy, or phenyl,

U is N or CR^1 , wherein R^1 is H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, or phenyl optionally substituted with a C_{1-6} alkyl, C_{1-6} alkoxy, or phenyl,

W is O, S or NR⁴, wherein R⁴ is H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, or phenyl optionally substituted with a C_{1-6} alkyl, C_{1-6} alkoxy, or phenyl.

27 (Previously presented). The method of claim 20, wherein the nucleophile is selected from Cl⁻, Br⁻, I⁻, or NC-S⁻.

28 (Previously presented). The method of claim 26, wherein the reagent of formula (6b) is selected from an isocyanate, an isothiocyanate, or a ketene.

29 (Previously presented). The method of claim 20, wherein a compound of formula (5) is first protected as a carbonate or carbamate and then reacted with the reagent of formula (6b) in step c2).

30 (Previously presented). The method of claim 20, wherein the nucleophile in step d2) is a soft nucleophile in an aqueous or organic solution.

31 (Currently amended). The method of claim 20, wherein the reaction with a nucleophile in step d2) is followed by acidification by adjusting pH to $[[\le 5]] \le 5$.

32 (Previously presented). The method of claim 20, wherein in step d2), reaction with the nucleophile in an aqueous solution is followed by separating the aqueous phase, followed by acidification with an aqueous acid, and extraction into an organic phase.

33 (Previously presented). The method of claim 20, wherein, prior to step e2), a compound of formula (8b) or a salt thereof is purified by the process of extraction from one phase to another.

34 (Currently amended). The method of claim 20, wherein in step d2), a compound of formula (8b) is obtained in high at a purity of more than 98% according to HPLC.

35 (Previously presented). The method of claim 20, wherein step e2) is carried out using a mineral acid.

36 (Currently amended). A method of preparing THIP 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol comprising reacting a compound of formula (8b) or a salt thereof

wherein, R is C_{1-12} alkyl, C_{2-12} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, or aryl optionally substituted with one or more C_{1-12} alkyl, C_{1-12} alkoxy, or aryl,

U' is NH or CHR¹, wherein R¹ is H or R,

W is O, S or NR⁴, wherein R⁴ is H or R,

with an acid to obtain THHP 4.5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol as an acid addition salt.

37 (Previously presented). A compound of formula (8b)

wherein R is C_{1-12} alkyl, C_{2-12} alkenyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, acyl, or aryl optionally substituted with one or more C_{1-12} alkyl, C_{1-12} alkoxy, or aryl,

U' is NH or CHR^{1} , wherein R^{1} is H or R,

W is O, S or NR⁴, wherein R⁴ is H or R, or a salt thereof.